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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	PAPER NUMBER
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/820,215	**Applicant(s)** BENJAMIN ET AL.	
	Examiner Brenda L. Coleman	**Art Unit** 1624	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 05 April 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *05 April 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): see attached.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-56*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Brenda Coleman

Brenda L. Coleman
Primary Examiner
Art Unit: 1624

ADVISORY ACTION

Claims 1-56 are pending in the application.

The period for reply continues to run FOUR MONTHS from the date of the final rejection. Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a) accompanied by the appropriate fee. The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. A reply within the meaning of 37 CFR 1.113 or a request for a continued examination (RCE) in compliance with 37 CFR 1.114 must be timely filed to avoid abandonment of this application.

The amendment filed April 5, 2007 under 37 CFR 1.116 in reply to the final rejection has been entered, but is not deemed to place the application in condition for allowance. For purposes of appeal, the status of the claims is as follows:

Allowed claim(s): NONE

Rejected claim(s): 1-56

Claim(s) objected to: NONE

This action is in response to applicant's amendment dated April 5, 2007.

Response to Arguments

1. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 1-56 labeled paragraph 1 of the last office action, the applicants' arguments have been fully considered, however they were not found persuasive. Applicants' state that a number of review articles that were previously submitted provide a recognized correlation

between antagonism at the NMDA receptors and the specified diseases and conditions set forth in the claims. However, the review articles of Wood, heresco-Levy, Bergink and Brown are not prior art and thus do not exhibit the state of the art prior to the filing of the instant application.

As stated in the previous office action, Trujillo does not state that NMDA receptor antagonists **prevent** the tolerance to opiate analgesia. Additionally, Brown et al., Current Topics in Medicinal Chemistry states that the study of NMDA antagonists in a variety of neuropathic pain models only suggests that they **may be** useful for **treating** the pathological conditions underlying neuropathic pain. While the specific diseases listed in claims 10, 13, 14, 16, 18, 20, 22, 24, 42, 44, 45, 47, 49, 51 and 53 have been indicated by the applicants to have a nexus with NMDA, this does not provide enablement for those diseases and/or disorders listed. Not all diseases and/or disorders are treatable, let alone preventable. Where structure sensitivity exists (in the pharmaceutical art) degree of testing must be representative of claims' scope. Note In re Fisher 166 USPQ 18; In re Surrey 151 USPQ 724. The recent journal article, i.e. Brown et al. (2006), provided by the applicant in their response filed September 6, 2006 indicates that deleterious side-effects observed with many of the compounds in clinical trials have raised the question if this is a mechanism-based effect which cannot be overcome. Furthermore, Brown states that it appears that within the non-competitive class of NMDA receptor antagonists, the most potent compound (e.g. MK-801) are unsuitable for clinical use due to the side effect profile.

While Brown et al., indicates that the use of memantine a clinically available (Parkinson's disease and more recently Alzheimer's disease) NMDA antagonist has demonstrated a superior side-effect profile, but did not show efficacy in several models of clinical pain. Thus the uses being urged are not in currently available form based on the activity relied on and the specification provides only a starting point for further research. Note Genentech vs. Novo Nordisk 42 USPQ 2d 1001.

Claims 1-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

2. With regards to the 35 U.S.C. § 112, second paragraph rejection labeled 2a) of the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive.

a) The applicant's stated that with respect to the phrase "pain relieving agent" a skilled artisan would have no difficulty understanding the meaning of the phrase. The phrase "pain relieving agent" is unduly functional. Names, structures, and chemical Formulae precisely define organic molecules. Attempting to define structure by function is not proper when the structures can be clearly expressed in terms that are more precise. Additionally, it is not sufficient to define a chemical structure solely by its principal biological property. The scope of compounds associated with pain relieving agent could alter over

time. The applicants' are not entitled to preempt the efforts of others. The claims are directed to a compositions and method of use of the compounds of the instant invention and an additional active ingredient, that is the applicants have not set forth the metes and bounds of the claim.

Claims 25 and 54 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and stated above.

3. With regards to the 35 U.S.C. § 102(b) anticipation rejection of claims 1-26 by LIN, labeled paragraph 5) in the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive. The applicants' stated that EP-B1-0,778,023 only discloses the use of rapamycin intranasally and also discloses that the product contains an NMDA antagonist such as [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-l(7)-en-2-yl)ethyl] phosphonic acid (EAA-090). The applicants' also stated that while EP-B1-0,778,023 discloses that the rapamycin may be administered intranasally, it further indicates that the NMDA antagonist does not necessarily need to administered at the same time and that even if the rapamycin and the NMDA antagonist are administered at the same time, this does not necessarily require that the compounds administered in the same manner. However, EP-B1-0,778,023 does not state that they cannot be administered at the same time. The claim language of the instant invention is such that the composition and method of use are open ended and the present of additional active ingredients is not precluded from the composition as claimed herein.

Claims 1-26 are rejected under 35 U.S.C. 102(b) as being anticipated by LIN et al., EP 0 778 023, for reasons of record and stated above.

4. With regards to the provisional obviousness-type double patenting rejection as being unpatentable over copending Application No. 10/969,715 of the last office action, the applicants requested that this rejection be held in abeyance at this time.

Claims 1-9 and 26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26-29 of copending Application No. 10/969,715, for reasons of record.

5. With regards to the provisional obviousness-type double patenting rejection as being unpatentable over copending Application No. 10/820,216 of the last office action, the applicants requested that this rejection be held in abeyance at this time.

Claims 27-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-28 of copending Application No. 10/820,216, for reasons of record.

6. With regards to the provisional obviousness-type double patenting rejection as being unpatentable over copending Application No. 10/961,871 of the last office action, the applicants requested that this rejection be held in abeyance at this time.

Claims 27-56 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-95 and 104-108 of copending Application No. 10/961,871, for reasons of record.

7. With regards to the provisional obviousness-type double patenting rejection as being unpatentable over copending Application No. 10/267,159 of the last office action, the applicants requested that this rejection be held in abeyance at this time.

Claims 21-24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 37-53 and 57-73 of copending Application No. 10/267,159, for reasons of record.

8. The applicants' amendments and arguments are sufficient to overcome the 35 USC § 112, second paragraph rejections labeled paragraph 2b), c) and d) of the last office action, which are hereby **withdrawn**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brenda Coleman

Brenda L. Coleman
Primary Examiner Art Unit 1624
April 17, 2007